

**What is Claimed is:**

1. An isolated human RNase polypeptide comprising human Type 2 RNase H.
2. The isolated human RNase polypeptide of claim 1 wherein the polypeptide comprises SEQ ID NO: 1.
3. An isolated human RNase polypeptide prepared from a culture of ATCC Deposit No. 98536.
4. A cloned and expressed human RNase H polypeptide.
5. The cloned and expressed human RNase H polypeptide of claim 4 which is a human Type 2 RNase H polypeptide.
6. The cloned and expressed human RNase H polypeptide of claim 4 which is a human RNase H1 polypeptide.
7. The cloned and expressed human RNase H polypeptide of claim 4 which comprises SEQ ID NO: 1.
- 15 8. The cloned and expressed human RNase H polypeptide of claim 4 which is prepared from a culture of ATCC Deposit No. 98536.
9. A composition comprising a cloned and expressed human RNase H polypeptide and a pharmaceutically acceptable carrier.
- 20 10. The composition of claim 9 wherein the human RNase H polypeptide is a human Type 2 RNase H polypeptide.
11. The composition of claim 9 wherein the human RNase H polypeptide is a human RNase H1 polypeptide.

12. A composition comprising a human RNase H polypeptide and a pharmaceutically acceptable carrier.

13. The composition of claim 12 further comprising an antisense oligonucleotide, wherein the human RNase H 5 polypeptide is a human Type 2 polypeptide.

14. An isolated polynucleotide encoding a human RNase H polypeptide.

15. The isolated polynucleotide of claim 14 which is a human Type 2 RNase H.

10 16. A vector comprising a nucleic acid encoding a human RNase H polypeptide.

17. A host cell comprising the vector of claim 16.

18. A composition comprising a vector comprising a nucleic acid encoding a human RNase H polypeptide and a 15 pharmaceutically acceptable carrier.

19. The composition of claim 18 further comprising an antisense oligonucleotide, wherein the human RNase H polypeptide is a human Type 2 RNase H polypeptide.

20. An antibody targeted to a human Type 2 RNase H 20 polypeptide.

21. A nucleic acid probe capable of hybridizing to a portion of a nucleic acid encoding a human Type 2 RNase H polypeptide.

22. A human Type 2 RNase H--his-tag fusion polypeptide.

23. An antisense oligonucleotide capable of eliciting cleavage of its complementary target RNA by a human Type 2 RNase H polypeptide wherein said human Type 2 RNase H polypeptide comprises SEQ ID NO: 1.

5 24. A method of enhancing inhibition of expression of a selected protein by an antisense oligonucleotide targeted to an RNA encoding the selected protein comprising:

(a) providing an antisense oligonucleotide targeted to an RNA encoding a selected protein whose expression is to be  
10 inhibited;

(b) allowing said oligonucleotide and said RNA to hybridize to form an oligonucleotide-RNA duplex;

15 (c) contacting said oligonucleotide-RNA duplex with a human Type 2 RNase H polypeptide, under conditions in which cleavage of the RNA strand of the oligonucleotide-RNA duplex occurs,

whereby inhibition of expression of the selected protein is enhanced.

25. The method of claim 24 wherein the human Type 2  
20 RNase H polypeptide comprises SEQ ID NO: 1.

26. The method of claim 25 wherein the antisense oligonucleotide is a chimeric oligonucleotide.

27. A method of screening oligonucleotides to identify an effective antisense oligonucleotide for inhibition of  
25 expression of a selected target protein comprising:

(a) contacting a human Type 2 RNase H polypeptide with an RNA encoding the selected target protein and an oligonucleotide complementary to at least a portion of the RNA under conditions in which an oligonucleotide-RNA duplex is  
30 formed;

(b) detecting cleavage of the RNA of the oligonucleotide-RNA duplex wherein cleavage is indicative of antisense efficacy.

28. The method of claim 27 wherein the human Type 2 RNase H polypeptide is enriched or overexpressed.

29. The method of claim 27 wherein the human Type 2 RNase H polypeptide is exogenously added.

30. The method of claim 27 wherein the human Type 2 RNase H polypeptide is an isolated, purified human Type 2 RNase H polypeptide.

31. An effective antisense oligonucleotide identified in accordance with the method of claim 27.

32. The method of claim 27 further comprising determining the site on the RNA at which cleavage occurs, whereby said site is identified as a Type 2 RNase H-sensitive site.

33. The method of claim 32 further comprising identifying an effective antisense oligonucleotide which hybridizes to said Type 2 RNase H-sensitive site.

20 34. The method of claim 27 wherein the oligonucleotide is one of a mixture or library of oligonucleotides.

35. An effective antisense oligonucleotide identified in accordance with the method of claim 33.

25 36. A method of making an antisense oligonucleotide which elicits cleavage of its complementary target RNA by a human Type 2 RNase H polypeptide comprising synthesizing an

oligonucleotide which is targeted to a selected RNA wherein said oligonucleotide,  
when hybridized to the selected RNA target to form a duplex,  
will bind the human Type 2 RNase H polypeptide which thereby  
5 cleaves the RNA strand of the duplex.

37. A method of prognosticating efficacy of antisense therapy of a selected disease comprising measuring the level or activity of a human Type 2 RNase H in a target cell of the antisense therapy.

10 38. A method of identifying agents which increase or decrease activity of levels of a human RNase H polypeptide in a host cell comprising:

15 (a) contacting a cell expressing a human RNase H polypeptide with an agent suspected or increasing or decreasing activity or levels of the human RNase H polypeptide; and

20 (b) measuring the activity or levels of the human RNase H polypeptide in the presence and absence of the agent so that an increase or decrease in the activity or levels of the human RNase H polypeptide can be determined.

39. A method of identifying agents which increase or decrease activity or levels of an RNase H polypeptide comprising:

25 a) contacting an RNase H polypeptide with an agent suspected of increasing or decreasing activity or levels of said RNase H polypeptide.

30 b) measuring the activity or levels of the RNase H polypeptide in the presence and absence of the agent so that an increase or decrease in the activity or levels of the human RNase H polypeptide can be determined.

40. The method of claim 39 wherein the RNase H polypeptide is a cloned and expressed RNase H polypeptide.

41. The method of claim 39 wherein the RNase H polypeptide is a human RNase H polypeptide.

5 42. The method of claim 39 wherein the RNase H polypeptide is a human RNase H polypeptide having SEQ ID NO: 1.

10 43. The method of claim 39 wherein the RNase H polypeptide is prepared from a culture of ATCC Deposit No. 98536.

15 44. A method of making substantially pure human Type 2 RNase H comprising transfecting a host cell with a vector containing a nucleic acid sequence encoding human Type 2 RNase H, wherein said host cells express the human Type 2 RNase H polypeptide, and isolating the human Type 2 RNase H polypeptide.

45. The method of claim 44 wherein said human Type 2 RNase polypeptide comprises SEQ ID NO: 1.